

=> e smith daniel j/au

E1	8	SMITH DANIEL H/AU
E2	2	SMITH DANIEL I/AU
E3	301 -->	SMITH DANIEL J/AU
E4	1	SMITH DANIEL JAMES/AU
E5	1	SMITH DANIEL JOHANNES/AU
E6	23	SMITH DANIEL JOHN/AU
E7	2	SMITH DANIEL JORDAN/AU
E8	4	SMITH DANIEL JOSEPH/AU
E9	13	SMITH DANIEL K/AU
E10	5	SMITH DANIEL KEITH/AU
E11	4	SMITH DANIEL L/AU
E12	3	SMITH DANIEL L JR/AU

=> s e3-e8 and (glucan or glucosyltransferase?)

L1 79 ("SMITH DANIEL J"/AU OR "SMITH DANIEL JAMES"/AU OR "SMITH DANIEL JOHANNES"/AU OR "SMITH DANIEL JOHN"/AU OR "SMITH DANIEL JORDAN"/AU OR "SMITH DANIEL JOSEPH"/AU) AND (GLUCAN OR GLUCOSYLTRANSFERASE?)

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 48 DUP REM L1 (31 DUPLICATES REMOVED)

=> s l2 and ((GbpB)or(glucan binding protein B))

L3 8 L2 AND ((GBP) OR (GLUCAN BINDING PROTEIN B))

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2005:498381 BIOSIS

DN PREV200510279091

TI Characterization of salivary immunoglobulin A responses in children heavily exposed to the oral bacterium Streptococcus mutans: Influence of specific antigen recognition in infection.

AU Nogueira, Ruche D.; Alves, Alessandra C.; Napimoga, Marcelo H.;

Smith, Daniel J.; Mattos-Graner, Renata O. [Reprint Author]

CS UNICAMP, Fac Odontol Piracicaba, Dept Microbiol and Immunol, Piracicaba Sch Dent, Av Limeira 901, BR-13414903 Sao Paulo, Brazil

rmgraner@fop.unicamp.br

SO Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5675-5684.

CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 16 Nov 2005

Last Updated on STN: 16 Nov 2005

AB The initial infection of children by Streptococcus mutans, the main pathogen of dental caries, depends on the ability of S. mutans to adhere and accumulate on tooth surfaces. These processes involve the adhesin antigen I/II (AgI/II), glucosyltransferases (GTF) and glucan-binding protein B (

GbpB), each a target for anticaries vaccines. The salivary immunoglobulin A (IgA) antibody responses to S. mutans antigens (Ags) were characterized in 21 pairs of 5- to 13-month-old children. Pairs were constructed with one early S. mutans-infected and one noninfected child matched by age, racial background, number of teeth, and salivary levels of IgA. Specific salivary IgA antibody response and S. mutans infection levels were then measured during a 1-year follow-up. Robust responses to S. mutans were detected from 6 months of age. Salivary IgA antibody to AgI/II and GTF was commonly detected in salivas of all 42 children.

However, GbpB-specific IgA antibody was seldom detected in the subset of infected children (38.1% at baseline). In contrast, most of the subset of noninfected children (76.2%) showed GbpB-reactive IgA antibody during the same period. Frequencies of GbpB responses increased with age, but differences in intensities of GbpB-IgA antibody reactions were sustained between the subsets. At baseline, GbpB-reactive IgA antibody accounted for at least half of the

total salivary IgA *S. mutans*-reactive antibody in 33.3 and 9.5% of noninfected and infected children, respectively. This study provides evidence that a robust natural response to *S. mutans* Ags can be achieved by 1 year of age and that IgA antibody specificities may be critical in modulating initial *S. mutans* infection.

L3 ANSWER 2 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2005:278296 BIOSIS
DN PREV200510068959
TI Immunological and protective effects of diepitopic subunit dental caries vaccines.
AU **Smith, Daniel J.** [Reprint Author]; King, William F.; Rivero, Joy; Taubman, Martin A.
CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org
SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from *mutans streptococcal glucosyltransferases* (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class II binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with *Streptococcus mutans* strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with *Streptococcus sobrinus* strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB**-derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both *S. mutans* and *S. sobrinus*.

L3 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:172182 BIOSIS
DN PREV200300172182
TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of *Streptococcus mutans glucan-binding protein B*.
AU **Smith, Daniel J.** [Reprint Author]; King, William F.; Barnes, Leigh A.; Peacock, Zachary; Taubman, Martin A.
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Apr 2003

AB

Glucan-binding protein B (

GbpB) from *Streptococcus mutans* has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the **gbpB** gene, our objective in this study was to identify immunogenic regions within the **GbpB** sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the **GbpB** sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact **GbpB**, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of *S. mutans* was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with *S. mutans* strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of **GbpB**, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L3 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:543227 BIOSIS
DN PREV200100543227

TI Cloning of the *Streptococcus mutans* gene encoding **glucan binding protein B** and analysis of genetic diversity and protein production in clinical isolates.

AU Mattos-Graner, Renata O.; Jin, Song; King, William F.; Chen, Tsute; Smith, Daniel J.; Duncan, Margaret J. [Reprint author]

CS Department of Molecular Genetics, Forsyth Institute, 140 Fenway, Boston, MA, 02115, USA
mduncan@forsyth.org

SO Infection and Immunity, (November, 2001) Vol. 69, No. 11, pp. 6931-6941. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 21 Nov 2001

Last Updated on STN: 25 Feb 2002

AB *Streptococcus mutans*, the primary etiological agent of dental caries, produces several activities that promote its accumulation within the dental biofilm. These include **glucosyltransferases**, their **glucan** products, and proteins that bind **glucan**. At least three **glucan** binding proteins have been identified, and **GbpB**, the protein characterized in this study, appears to be novel. The **gbpB** gene was cloned and the predicted protein sequence contained several unusual features and shared extensive homology with a putative peptidoglycan hydrolase from group B streptococcus. Examination of **gbpB** genes from clinical isolates of *S. mutans* revealed that DNA polymorphisms, and hence amino acid changes, were limited to the central region of the gene, suggesting functional conservation within the amino and carboxy termini of the protein. The **GbpB** produced by clinical isolates and laboratory strains showed various distributions between cells and culture medium, and amounts of protein produced by individual strains correlated positively with their ability to grow as biofilms in an in vitro assay.

L3 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:303013 BIOSIS
DN PREV200100303013

TI Passive transfer of immunoglobulin Y antibody to *Streptococcus mutans* **glucan binding protein B** can confer protection against experimental dental caries.

AU **Smith, Daniel J.** [Reprint author]; King, William F.; Godiska, Ronald

CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org

SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 3135-3142. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Active immunization with *Streptococcus mutans* **glucan binding protein B** (GBP-B) has been shown to induce protection against experimental dental caries. This protection presumably results from continuous secretion of salivary antibody to GBP-B, which inhibits accumulation of *S. mutans* within the oral biofilm. The purpose of this study was to explore the influence of short-term (9- or 24-day) passive oral administration of antibody to *S. mutans* GBP-B on the longer-term accumulation and cariogenicity of *S. mutans* in a rat model of dental caries. Preimmune chicken egg yolk immunoglobulin Y (IgY) or IgY antibody to *S. mutans* GBP-B was supplied in lower (experiment 1) and higher (experiment 2) concentrations in the diet and drinking water of rats for 9 (experiment 1) or 24 (experiment 2) days. During the first 3 days of IgY feeding, all animals were challenged with 5X10⁶ streptomycin-resistant *S. mutans* strain SJ-r organisms. Rats remained infected with *S. mutans* for 78 days, during which rat molars were sampled for the accumulation of *S. mutans* SJ-r bacteria and total streptococci. Geometric mean levels of *S. mutans* SJ-r accumulation on molar surfaces were significantly lower in antibody-treated rats on days 16 and 78 of experiment 2 and were lower on all but the initial (day 5) swabbing occasions in both experiments. Relative to controls, the extent of molar dental caries measured on day 78 was also significantly decreased. The decrease in molar caries correlated with the amount and duration of antibody administration. This is the first demonstration that passive antibody to *S. mutans* GBP-B can have a protective effect against cariogenic *S. mutans* infection and disease. Furthermore, this decrease in infection and disease did not require continuous antibody administration for the duration of the infection period. This study also indicates that antibody to components putatively involved only in cellular aggregation can have a significant effect on the incorporation of *mutans streptococci* in dental biofilm.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:122595 CAPLUS

DN 142:217367

TI Immunogenic compositions for eliciting antibody production in mammals composed of fragments of *Streptococcus* **glucan binding protein-B** and **glucosyltransferase** isoenzymes

IN **Smith, Daniel J.**; Taubman, Martin A.

PA USA

SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 2005031633	A1	20050210	US 2004-797821	20040309
	US 6827936	B1	20041207	US 1999-290049	19990412
	US 2004127400	A1	20040701	US 2003-383930	20030307
PRAI	US 1998-81550P	P	19980413		
	US 1999-115142P	P	19990108		
	US 1999-290049	A2	19990412		
	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	US 2003-383930	A2	20030307		

AB The invention provides complete and partial sequences of various **GbpB (glucan binding protein-B)** proteins and **glucosyltransferase (GTF)** isoenzymes found in *Streptococcus* species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of *Streptococcus GbpB* and a biocompatible microparticle; or (b) fragments of *Streptococcus GbpB* and GTF isoenzymes and a biocompatible microparticle. The invention relates that the **GbpB-GTF** composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed **GbpB-GTF** chimeric protein may also contain a plurality of copies of the **GbpB** and GTF peptides. The invention also provides two specific **GbpB-GTF** diepitopic chimeric proteins: (a) SYI-GLU, which comprises *S. mutans* strain SJ32 **GbpB**-derived MHC class II SYI peptide and the **glucan** binding domain of GTF; and (b) SYI-CAT, which comprises *S. mutans* strain SJ32 **GbpB**-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and **GbpB**. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with *S. mutans GbpB* peptide SYI.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:737524 CAPLUS

DN 139:259950

TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries

IN Smith, Daniel J.; Taubman, Martin A.

PA The Forsyth Institute, USA

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075845	A2	20030918	WO 2003-US6962	20030307
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480962	AA	20030918	CA 2003-2480962	20030307
	EP 1572149	A2	20050914	EP 2003-713953	20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	WO 2003-US6962	W	20030307		

AB Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to *S. mutans glucan binding protein-B* or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding**

protein-B or glucosyltransferase.

L3 ANSWER 8 OF 8 USPATFULL on STN
AN 2004:165910 USPATFULL
TI Immunogenicity of **glucan** binding protein
IN **Smith, Daniel J.**, Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
PI US 2004127400 A1 20040701
AI US 2003-383930 A1 20030307 (10)
PRAI US 2002-402483P 20020808 (60)
US 2002-363209P 20020307 (60)
DT Utility
FS APPLICATION
LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and
Popeo, P.C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 3002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunogenic compositions and subunit vaccines for dental caries are
described which comprise peptide subunits of **glucan**
binding protein-B and peptide subunits of
glucan binding protein-B in
combination with peptide subunits of **glucosyltransferase**.
Methods of provoking an immune response to *S. mutans* **glucan**
binding protein-B or
glucosyltransferase. Methods of immunizing a mammal against
dental caries are also described, along with antibodies which bind
particular epitopes of **glucan binding**
protein-B or **glucosyltransferase**.

=> e taubman martin A/au

E1	195	TAUBMAN MARK B/AU
E2	4	TAUBMAN MARTIN/AU
E3	121 -->	TAUBMAN MARTIN A/AU
E4	1	TAUBMAN MATTHEW/AU
E5	19	TAUBMAN MATTHEW S/AU
E6	6	TAUBMAN MICHELE/AU
E7	1	TAUBMAN MITCHELL/AU
E8	1	TAUBMAN N A/AU
E9	1	TAUBMAN NORA E/AU
E10	2	TAUBMAN O/AU
E11	14	TAUBMAN P/AU
E12	1	TAUBMAN P D/AU

=> s e2-e3 and (glucan or glucosyltransferase?)

L4 63 ("TAUBMAN MARTIN"/AU OR "TAUBMAN MARTIN A"/AU) AND (GLUCAN OR
GLUCOSYLTRANSFERASE?)

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 40 DUP REM L4 (23 DUPLICATES REMOVED)

=> s l5 and ((GbpB)or(glucan binding protein B))

L6 5 L5 AND ((GBPB) OR(GLUCAN BINDING PROTEIN B))

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2005:278296 BIOSIS
DN PREV200510068959
TI Immunological and protective effects of diepitopic subunit dental caries
vaccines.
AU **Smith, Daniel J.** [Reprint Author]; King, William F.; Rivero, Joy;
Taubman, Martin A.

CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org
SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from mutans streptococcal **glucosyltransferases** (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class II binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with *Streptococcus mutans* strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with *Streptococcus sobrinus* strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB**-derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both *S. mutans* and *S. sobrinus*.

L6 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:172182 BIOSIS
DN PREV200300172182
TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of *Streptococcus mutans* **glucan-binding protein B**.
AU Smith, Daniel J. [Reprint Author]; King, William F.; Barnes, Leigh A.; Peacock, Zachary; **Taubman, Martin A.**
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print. ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003
AB **Glucan-binding protein B** (**GbpB**) from *Streptococcus mutans* has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the **gbpB** gene, our objective in this study was to identify immunogenic regions within the **GbpB** sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the **GbpB** sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A

preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact **GbpB**, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of *S. mutans* was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with *S. mutans* strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of **GbpB**, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:122595 CAPLUS
 DN 142:217367
 TI Immunogenic compositions for eliciting antibody production in mammals composed of fragments of *Streptococcus* **glucan binding protein-B** and **glucosyltransferase** isoenzymes
 IN Smith, Daniel J.; Taubman, Martin A.
 PA USA
 SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930. CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005031633	A1	20050210	US 2004-797821	20040309
	US 6827936	B1	20041207	US 1999-290049	19990412
	US 2004127400	A1	20040701	US 2003-383930	20030307
PRAI	US 1998-81550P	P	19980413		
	US 1999-115142P	P	19990108		
	US 1999-290049	A2	19990412		
	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	US 2003-383930	A2	20030307		
AB	<p>The invention provides complete and partial sequences of various GbpB (glucan binding protein-B) proteins and glucosyltransferase (GTF) isoenzymes found in <i>Streptococcus</i> species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of <i>Streptococcus GbpB</i> and a biocompatible microparticle; or (b) fragments of <i>Streptococcus GbpB</i> and GTF isoenzymes and a biocompatible microparticle. The invention relates that the GbpB-GTF composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed GbpB-GTF chimeric protein may also contain a plurality of copies of the GbpB and GTF peptides. The invention also provides two specific GbpB-GTF diepitopic chimeric proteins: (a) SYI-GLU, which comprises <i>S. mutans</i> strain SJ32 GbpB-derived MHC class II SYI peptide and the glucan binding domain of GTF; and (b) SYI-CAT, which comprises <i>S. mutans</i> strain SJ32 GbpB-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and GbpB. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with <i>S. mutans GbpB</i> peptide SYI.</p>				

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2003:737524 CAPLUS

DN 139:259950
 TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries
 IN Smith, Daniel J.; **Taubman, Martin A.**
 PA The Forsyth Institute, USA
 SO PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075845	A2	20030918	WO 2003-US6962	20030307
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480962	AA	20030918	CA 2003-2480962	20030307
	EP 1572149	A2	20050914	EP 2003-713953	20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	WO 2003-US6962	W	20030307		
AB	Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of glucan binding protein-B and peptide subunits of glucan binding protein-B in combination with peptide subunits of glucosyltransferase . Methods of provoking an immune response to <i>S. mutans</i> glucan binding protein-B or glucosyltransferase . Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of glucan binding protein-B or glucosyltransferase .				

L6 ANSWER 5 OF 5 USPATFULL on STN
 AN 2004:165910 USPATFULL
 TI Immunogenicity of **glucan binding protein**
 IN Smith, Daniel J., Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
 PI US 2004127400 A1 20040701
 AI US 2003-383930 A1 20030307 (10)
 PRAI US 2002-402483P 20020808 (60)
 US 2002-363209P 20020307 (60)
 DT Utility
 FS APPLICATION
 LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA, 02111
 CLMN Number of Claims: 32
 ECL Exemplary Claim: 1
 DRWN 12 Drawing Page(s)
 LN.CNT 3002
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Immunogenic compositions and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to *S. mutans* **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against

dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

=> s (glucan or glucosyltransferase?) and ((glucan binding protein B) or (GbpB))
L7 56 (GLUCAN OR GLUCOSYLTRANSFERASE?) AND ((GLUCAN BINDING PROTEIN B)
OR (GBPB))

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 18 DUP REM L7 (38 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 18 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 18 MEDLINE on STN DUPLICATE 1
AN 2006005869 IN-PROCESS
DN PubMed ID: 16390340
TI Binding of **glucan**-binding protein C to GTFD-synthesized soluble **glucan** in sucrose-dependent adhesion of Streptococcus mutans.
AU Matsumoto M; Fujita K; Ooshima T
CS Department of Pediatric Dentistry, Osaka University Graduate School of Dentistry, Osaka, Japan.
SO Oral microbiology and immunology, (2006 Feb) 21 (1) 42-6.
Journal code: 8707451. ISSN: 0902-0055.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Dental Journals
ED Entered STN: 20060105
Last Updated on STN: 20060105
AB Streptococcus mutans produces **glucan**-binding proteins (Gbp proteins) which promote the adhesion of the organism to teeth. Three Gbp proteins, GbpA protein, **GbpB** protein, and GbpC protein have been identified; however, the mechanism of adhesion between glucans and bacterial cell surfaces is unknown. We used **glucosyltransferase** (GTF)- and/or Gbp-deficient mutants to examine the role of GbpC protein in the sucrose-dependent cellular adhesion of S. mutans to glass surfaces. The wild-type strain MT8148 and a GbpA-deficient mutant strain displayed increased sucrose-dependent adhesion following the addition of rGTFD. However, a GbpC-deficient mutant strain demonstrated no changes in the level of sucrose-dependent adhesion in spite of the addition of rGTFD. Further, the binding of rGbpC protein to the **glucan** synthesized by rGTFD was significantly higher than that to the **glucan** synthesized by either rGTFB or rGTFC. These results suggest that GbpC protein may play an important role in sucrose-dependent adhesion by binding to the soluble **glucan** synthesized by GTFD.

L8 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2005:122595 CAPLUS
DN 142:217367
TI Immunogenic compositions for eliciting antibody production in mammals composed of fragments of Streptococcus **glucan binding protein-B** and **glucosyltransferase** isoenzymes
IN Smith, Daniel J.; Taubman, Martin A.
PA USA
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005031633	A1	20050210	US 2004-797821	20040309
	US 6827936	B1	20041207	US 1999-290049	19990412
	US 2004127400	A1	20040701	US 2003-383930	20030307
PRAI	US 1998-81550P	P	19980413		
	US 1999-115142P	P	19990108		

US 1999-290049 A2 19990412
US 2002-363209P P 20020307
US 2002-402483P P 20020808
US 2003-383930 A2 20030307

AB The invention provides complete and partial sequences of various **GbpB (glucan binding protein-B)** proteins and **glucosyltransferase (GTF)** isoenzymes found in *Streptococcus* species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of *Streptococcus GbpB* and a biocompatible microparticle; or (b) fragments of *Streptococcus GbpB* and GTF isoenzymes and a biocompatible microparticle. The invention relates that the **GbpB-GTF** composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed **GbpB-GTF** chimeric protein may also contain a plurality of copies of the **GbpB** and GTF peptides. The invention also provides two specific **GbpB-GTF** diepitopic chimeric proteins: (a) SYI-GLU, which comprises *S. mutans* strain SJ32 **GbpB**-derived MHC class II SYI peptide and the **glucan** binding domain of GTF; and (b) SYI-CAT, which comprises *S. mutans* strain SJ32 **GbpB**-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and **GbpB**. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with *S. mutans GbpB* peptide SYI.

L8 ANSWER 3 OF 18 USPATFULL on STN
AN 2005:331878 USPATFULL
TI Computational method for identifying adhesin and adhesin-like proteins of therapeutic potential
IN Sachdeva, Gaurav, Delhi, INDIA
Kumar, Kaushal, Delhi, INDIA
Jain, Preti, Delhi, INDIA
Brahmachari, Samir K., Delhi, INDIA
Ramachandran, Srinivasan, Delhi, INDIA
PA COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH, New Delhi, INDIA
(non-U.S. corporation)
PI US 2005288866 A1 20051229
AI US 2005-52554 A1 20050207 (11)
PRAI IN 2004-1732004 20040206
US 2004-589227P 20040720 (60)
DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN LLP, 233 S. WACKER DRIVE, SUITE 6300, SEARS TOWER, CHICAGO, IL, 60606, US
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)

LN.CNT 1730

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A computational method for identifying adhesin and adhesin-like proteins, said method comprising steps of computing the sequence-based attributes of a neural network software wherein the attributes are (i) amino acid frequencies, (ii) multiplet frequency, (iii) dipeptide frequencies, (iv), charge composition, and (v) hydrophobic composition, training the artificial neural Network (ANN) for each of the computed five attributes, and identifying the adhesin and adhesin-like proteins having probability of being an adhesin (P.sub.ad) as ≥ 0.51 ; a computer system for performing the method; and genes and proteins encoding adhesin and adhesin-like proteins.

L8 ANSWER 4 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3
AN 2005:554664 BIOSIS
DN PREV200510340130

TI Role of HtrA in surface protein expression and biofilm formation by *Streptococcus mutans*.
 AU Biswas, Saswati; Biswas, Indranil [Reprint Author]
 CS Univ S Dakota, Sch Med, Div Basic Biomed Sci, Lee Med Bldg, 414 E Clark St, Vermillion, SD 57069 USA
 ibiswas@usd.edu
 SO Infection and Immunity, (OCT 2005) Vol. 73, No. 10, pp. 6923-6934.
 CODEN: INFIBR. ISSN: 0019-9567.
 DT Article
 LA English
 OS GenBank-AE004092; EMBL-AE004092; DDJB-AE004092; GenBank-AE015037; EMBL-AE015037; DDJB-AE015037; GenBank-NC004350; EMBL-NC004350; DDJB-NC004350; GenBank-NC003098; EMBL-NC003098; DDJB-NC003098; GenBank-NC002662; EMBL-NC002662; DDJB-NC002662
 ED Entered STN: 7 Dec 2005
 Last Updated on STN: 7 Dec 2005
 AB The HtrA surface protease in gram-positive bacteria is involved in the processing and maturation of extracellular proteins and degradation of abnormal or misfolded proteins. Inactivation of htrA has been shown to affect the tolerance to thermal and environmental stress and to reduce virulence. We found that inactivation of *Streptococcus mutans* htrA by gene-replacement also resulted in a reduced ability to withstand exposure to low and high temperatures, low pH, and oxidative and DNA damaging agents. The htrA mutation affected surface expression of several extracellular proteins including **glucan-binding protein B (GbpB)**, **glucosyltransferases**, and fructosyltransferase. In addition, htrA mutation also altered the surface expression of enolase and glyceraldehyde-3-phosphate dehydrogenase, two glycolytic enzymes that are known to be present on the streptococcal cell surface. As expected, microscopic analysis of in vitro grown biofilm structure revealed that the htrA deficient biofilms adopted a much more granular patchy appearance, rather than the relatively smooth confluent layer normally seen in the wild type. These results suggest that HtrA plays an important role in the biogenesis of extracellular proteins including surface associated glycolytic enzymes and in biofilm formation of *S. mutans*.

L8 ANSWER 5 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 4
 AN 2005:498381 BIOSIS
 DN PREV200510279091
 TI Characterization of salivary immunoglobulin A responses in children heavily exposed to the oral bacterium *Streptococcus mutans*: Influence of specific antigen recognition in infection.
 AU Nogueira, Ruchele D.; Alves, Alessandra C.; Napimoga, Marcelo H.; Smith, Daniel J.; Mattos-Graner, Renata O. [Reprint Author]
 CS UNICAMP, Fac Odontol Piracicaba, Dept Microbiol and Imunol, Piracicaba Sch Dent, Av Limeira 901, BR-13414903 Sao Paulo, Brazil
 rmgraner@fop.unicamp.br
 SO Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5675-5684.
 CODEN: INFIBR. ISSN: 0019-9567.
 DT Article
 LA English
 ED Entered STN: 16 Nov 2005
 Last Updated on STN: 16 Nov 2005
 AB The initial infection of children by *Streptococcus mutans*, the main pathogen of dental caries, depends on the ability of *S. mutans* to adhere and accumulate on tooth surfaces. These processes involve the adhesin antigen I/II (AgI/II), **glucosyltransferases** (GTF) and **glucan-binding protein B (GbpB)**, each a target for anticaries vaccines. The salivary immunoglobulin A (IgA) antibody responses to *S. mutans* antigens (Ags) were characterized in 21 pairs of 5- to 13-month-old children. Pairs were constructed with one early *S. mutans*-infected and one noninfected child matched by age, racial background, number of teeth, and salivary levels of IgA. Specific salivary IgA antibody response and *S. mutans* infection levels were then measured during a 1-year follow-up. Robust responses to *S. mutans* were detected from 6 months of age. Salivary IgA antibody to AgI/II and GTF was commonly detected in salivas of all 42 children.

However, **GbpB**-specific IgA antibody was seldom detected in the subset of infected children (38.1% at baseline). In contrast, most of the subset of noninfected children (76.2%) showed **GbpB**-reactive IgA antibody during the same period. Frequencies of **GbpB** responses increased with age, but differences in intensities of **GbpB**-IgA antibody reactions were sustained between the subsets. At baseline, **GbpB**-reactive IgA antibody accounted for at least half of the total salivary IgA *S. mutans*-reactive antibody in 33.3 and 9.5% of noninfected and infected children, respectively. This study provides evidence that a robust natural response to *S. mutans* Ags can be achieved by 1 year of age and that IgA antibody specificities may be critical in modulating initial *S. mutans* infection.

L8 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

AN 2005:531713 CAPLUS

DN 143:208717

TI A VicRK signal transduction system in *Streptococcus mutans* affects gtfBCD, **gbpB**, and ftf expression, biofilm formation, and genetic competence development

AU Senadheera, M. Dilani; Guggenheim, Bernard; Spatafora, Grace A.; Huang, Yi-Chen Cathy; Choi, Jison; Hung, David C. I.; Treglown, Jennifer S.; Goodman, Steven D.; Ellen, Richard P.; Cvitkovitch, Dennis G.

CS Dental Research Institute, University of Toronto, Toronto, ON, M51G6, Can.

SO Journal of Bacteriology (2005), 187(12), 4064-4076

CODEN: JOBAAY; ISSN: 0021-9193

PB American Society for Microbiology

DT Journal

LA English

AB Bacteria exposed to transient host environments can elicit adaptive responses by triggering the differential expression of genes via two-component signal transduction systems. This study describes the vicRK signal transduction system in *Streptococcus mutans*. A vicK (putative histidine kinase) deletion mutant (SmuvicK) was isolated. However, a vicR (putative response regulator) null mutation was apparently lethal, since the only transformants isolated after attempted mutagenesis overexpressed all three genes in the vicRKX operon (Smuvic+). Compared with the wild-type UA159 strain, both mutants formed aberrant biofilms. Moreover, the vicK mutant biofilm formed in sucrose-supplemented medium was easily detachable relative to that of the parent. The rate of total dextran formation by this mutant was remarkably reduced compared to the wild type, whereas it was increased in Smuvic+. Based on real-time PCR, Smuvic+ showed increased gtfBCD, **gbpB**, and ftf expression, while a recombinant VicR fusion protein was shown to bind the promoter regions of the gtfB, gtfC, and ftf genes. Also, transformation efficiency in the presence or absence of the *S. mutans* competence-stimulating peptide was altered for the vic mutants. In vivo studies conducted using SmuvicK in a specific-pathogen-free rat model resulted in significantly increased smooth-surface dental plaque (Pearson-Filon statistic [PF], < 0.001). While the absence of vicK did not alter the incidence of caries, a significant reduction in SmuvicK CFU counts was observed in plaque samples relative to that of the parent (PF, < 0.001). Taken together, these findings support involvement of the vicRK signal transduction system in regulating several important physiol. processes in *S. mutans*.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 6

AN 2005:278296 BIOSIS

DN PREV200510068959

TI Immunological and protective effects of diepitopic subunit dental caries vaccines.

AU Smith, Daniel J. [Reprint Author]; King, William F.; Rivero, Joy; Taubman, Martin A.

CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org

SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.

CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from mutans streptococcal **glucosyltransferases** (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class II binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with *Streptococcus mutans* strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with *Streptococcus sobrinus* strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB**-derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both *S. mutans* and *S. sobrinus*.

L8 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1342490 CAPLUS
TI Preliminary study of pcDNA3.1 (+)-**gbpB**-chitosan nanoparticles as a novel nasal delivery system for anti-cariou vaccine
AU Wei, Kewen; Fan, Mingwen; Wu, Buling
CS School of Stomatology, Wuhan University, Wuhan, 430079, Peop. Rep. China
SO Wuhan Daxue Xuebao, Yixueban (2005), 26(3), 351-354
CODEN: WDXYAA; ISSN: 1671-8852
PB Wuhan Daxue Qikanshe
DT Journal
LA Chinese
AB The effect of intranasal administration of pcDNA3.1 (+)-**gbpB**-chitosan nanoparticles on the systemic and mucosal immune response was examined. Two formulations of pcDNA3.1 (+)-**gbpB**-chitosan nanoparticles were prepared and administrated to immunize Sprague-Dawley (SD) rats through the nasal. Serum and salivary samples were collected periodically, **GbpB**-specific IgG and IgA antibodies were measured by an adapted method ELISA (ELISA). The system and local immune response were significantly higher than that observed as the neg. controls. The chitosan nanoparticles formulated in this study were suitable for the intranasal anti-cariou plasmid DNA vaccine delivery.

L8 ANSWER 9 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 7
AN 2005:132142 BIOSIS
DN PREV200500133041
TI Influence of microparticle formulation on immunogenicity of SYI, a synthetic peptide derived from *Streptococcus mutans* **GbpB**.
AU Peacock, Z. S.; Barnes, L. A.; King, W. F.; Trantolo, D. J.; Wise, D. L.; Taubman, M. A.; Smith, D. J. [Reprint Author]
CS Dept Immunol, Forsyth Inst, 140 Fenway, Boston, MA, 02115, USA
SO Oral Microbiology and Immunology, (February 2005) Vol. 20, No. 1, pp. 60-64. print.
ISSN: 0902-0055 (ISSN print).

DT Article
LA English
ED Entered STN: 6 Apr 2005
Last Updated on STN: 6 Apr 2005
AB Subcutaneous immunization with SYI, a peptide construct based on Streptococcus mutans **glucan binding protein B (GbpB)** residues 113-132, significantly reduces experimental dental caries. Since mucosal immunization may be preferred for human vaccine applications, the present objective was to determine what formulation of SYI combined with polylactide-coglycolide microparticles could give rise to significant levels of salivary IgA antibody reactive with the native **GbpB** protein. A comparison of the SYI construct, loaded into or mixed with polylactide-coglycolide revealed the SYI-loaded microparticles to induce significant and sustainable levels of salivary and nasal wash IgA antibody to the peptide and the native protein. SYI mixed with unloaded microparticles was less effective in mucosal antibody response induction. These studies indicate that mucosal immunization with the SYI construct can induce salivary IgA antibody to a pathogenesis-associated component of S. mutans if delivered within polylactide-coglycolide microparticles, suggesting that this approach could successfully induce protective salivary immunity to dental caries caused by S. mutans.

L8 ANSWER 10 OF 18 USPATFULL on STN
AN 2004:165910 USPATFULL
TI Immunogenicity of **glucan** binding protein
IN Smith, Daniel J., Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
PI US 2004127400 A1 20040701
AI US 2003-383930 A1 20030307 (10)
PRAI US 2002-402483P 20020808 (60)
US 2002-363209P 20020307 (60)
DT Utility
FS APPLICATION
LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 3002

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunogenic compositions and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

L8 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
AN 2005:197678 CAPLUS
DN 142:480327
TI Establishment of gene vaccine for caries prevention in the cells of mammals and its expression characteristics
AU Wei, Kewen; Wu, Buling; Xiao, Mingzhen; Su, Lingyun
CS College of Stomatology, Fourth Military Medical University, Xian, Shaanxi Province, 710032, Peop. Rep. China
SO Zhongguo Linchuang Kangfu (2004), 8(14), 2750-2751, 1 plate
CODEN: ZLKHAH; ISSN: 1671-5926
PB Zhongguo Linchuang Kangfu Zazhishe
DT Journal
LA English
AB The expression of **glucan-binding protein B (gbpB)** eukaryotic expression plasmid in the COS-7 cells of mammals was observed Eukaryotic expression plasmid pcDNA3.1(+)-

gbpB was established by gene recombinant technique, and was transfected into COS-7 cells by liposome method. The expression of plasmid pcDNA3.1(+)-**gbpB** in COS-7 cells was assayed by immunohistochem. SABC method and DAB staining. The cytoplasm of the COS-7 cells transfected by pcDNA3.1 (+)-**gbpB** plasmid showed a light brown staining, and there was no staining in the nucleus. There was no staining in the cytoplasm and nucleus of the cells transfected by pcDNA3.1(+) empty carrier as well as those in the control group. Plasmid pcDNA3.1(+)-**gbpB** can be translated and expressed in COS-7 cells after transfection. The expressed protein is in cytoplasm, and can bind with anti-**gbpB** specific antibody. Therefore, the plasmid pcDNA3.1(+)-**gbpB** with antigenicity can be used as a gene vaccine.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737524 CAPLUS
DN 139:259950

TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries

IN Smith, Daniel J.; Taubman, Martin A.

PA The Forsyth Institute, USA

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075845	A2	20030918	WO 2003-US6962	20030307
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480962	AA	20030918	CA 2003-2480962	20030307
	EP 1572149	A2	20050914	EP 2003-713953	20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	WO 2003-US6962	W	20030307		

AB Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

L8 ANSWER 13 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 9

AN 2003:172182 BIOSIS

DN PREV200300172182

TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of Streptococcus mutans **glucan-binding protein B**.

AU Smith, Daniel J. [Reprint Author]; King, William F.; Barnes, Leigh A.;

Peacock, Zachary; Taubman, Martin A.
 CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA,
 02115, USA
 dsmith@forsyth.org
 SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print.
 ISSN: 0019-9567 (ISSN print).
 DT Article
 LA English
 ED Entered STN: 2 Apr 2003
 Last Updated on STN: 2 Apr 2003
 AB **Glucan-binding protein B (GbpB)** from *Streptococcus mutans* has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the *gbpB* gene, our objective in this study was to identify immunogenic regions within the *GbpB* sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the *GbpB* sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact *GbpB*, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of *S. mutans* was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with *S. mutans* strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of *GbpB*, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L8 ANSWER 14 OF 18 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
 AN 2003014640 EMBASE
 TI Dental caries vaccines: Prospects and concerns.
 AU Smith D.J.
 CS D.J. Smith, Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA 02115, United States. dsmith@forsyth.org
 SO Critical Reviews in Oral Biology and Medicine, (2002) Vol. 13, No. 4, pp. 335-349.
 Refs: 155
 ISSN: 1045-4411 CODEN: CROME
 CY United States
 DT Journal; General Review
 FS 037 Drug Literature Index
 039 Pharmacy
 LA English
 SL English
 ED Entered STN: 20030116
 Last Updated on STN: 20030116
 AB Dental caries remains one of the most common infectious diseases of mankind. Cariogenic micro-organisms enter the dental biofilm early in life and can subsequently emerge, under favorable environmental conditions, to cause disease. In oral fluids, adaptive host defenses aroused by these infections are expressed in the saliva and gingival crevicular fluid. This review will focus on methods by which mucosal host defenses can be induced by immunization to interfere with dental caries caused by *mutans streptococci*. The natural history of *mutans streptococcal* colonization is described in the context of the ontogeny of mucosal immunity to these and other indigenous oral *streptococci*. Molecular targets for dental caries vaccines are explored for their

effectiveness in intact protein and subunit (synthetic peptide, recombinant and conjugate) vaccines in pre-clinical studies. Recent progress in the development of mucosal adjuvants and viable and non-viable delivery systems for dental caries vaccines is described. Finally, the results of clinical trials are reviewed, followed by a discussion of the prospects and concerns of human application of the principles presented.

L8 ANSWER 15 OF 18 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:592977 SCISEARCH
GA The Genuine Article (R) Number: 559KE
TI Mutant analysis of the gene encoding **glucan binding protein B** indicates an essential role in Streptococcus mutans
AU Mattos-Graner R O (Reprint); Zucchi P; Smith D J; Duncan M J
SO JOURNAL OF DENTAL RESEARCH, (MAR 2002) Vol. 81, Sp. iss. SI, pp. A40-A40. MA 0091.
ISSN: 0022-0345.
PB INT AMER ASSOC DENTAL RESEARCH I A D R/A A D R, 1619 DUKE ST, ALEXANDRIA, VA 22314-3406 USA.
DT Conference; Journal
LA English
REC Reference Count: 0
ED Entered STN: 2 Aug 2002
Last Updated on STN: 2 Aug 2002

L8 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:272625 BIOSIS
DN PREV200300272625
TI 80th General Session of the IADR, 31st Annual Meeting of the AADR, and the 26th Annual Meeting of the CADR, San Diego, California, USA, March 6-9, 2002.
AU Anonymous
SO Journal of Dental Research, (March 2002) Vol. 81, No. Special Issue A, pp. A1-A568. print.
Meeting Info.: 80th General Session of the IADR, 31st Annual Meeting of the AADR, and the 26th Annual Meeting of the CADR. San Diego, California, USA. March 06-09, 2002.
CODEN: JDREAF. ISSN: 0022-0345.
DT Conference; (Meeting)
Conference; (Meeting Summary)
LA English
ED Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003
AB This meeting on dental research consists of abstracts written in English for 4,155 presentations and posters. Session themes cover biocompatibility of dental materials, periodontal medicine during pregnancy, enamel proteins, risk factors for tooth loss, and saliva in health and disease. Selected topics include gene encoding **glucan -binding protein B**, anticancer effect of lentiviral vector, masticatory muscle activity, HIV-related dysplastic warts, and fungicidal activity of zinc.

L8 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:543227 BIOSIS
DN PREV200100543227
TI Cloning of the Streptococcus mutans gene encoding **glucan binding protein B** and analysis of genetic diversity and protein production in clinical isolates.
AU Mattos-Graner, Renata O.; Jin, Song; King, William F.; Chen, Tsute; Smith, Daniel J.; Duncan, Margaret J. [Reprint author]
CS Department of Molecular Genetics, Forsyth Institute, 140 Fenway, Boston, MA, 02115, USA
mduncan@forsyth.org
SO Infection and Immunity, (November, 2001) Vol. 69, No. 11, pp. 6931-6941. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article
LA English
ED Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002
AB Streptococcus mutans, the primary etiological agent of dental caries, produces several activities that promote its accumulation within the dental biofilm. These include **glucosyltransferases**, their **glucan** products, and proteins that bind **glucan**. At least three **glucan** binding proteins have been identified, and **GbpB**, the protein characterized in this study, appears to be novel. The **gbpB** gene was cloned and the predicted protein sequence contained several unusual features and shared extensive homology with a putative peptidoglycan hydrolase from group B streptococcus. Examination of **gbpB** genes from clinical isolates of *S. mutans* revealed that DNA polymorphisms, and hence amino acid changes, were limited to the central region of the gene, suggesting functional conservation within the amino and carboxy termini of the protein. The **GbpB** produced by clinical isolates and laboratory strains showed various distributions between cells and culture medium, and amounts of protein produced by individual strains correlated positively with their ability to grow as biofilms in an in vitro assay.

L8 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN DUPLICATE 11
AN 2001:303013 BIOSIS
DN PREV200100303013
TI Passive transfer of immunoglobulin Y antibody to Streptococcus mutans
glucan binding protein B can confer
protection against experimental dental caries.
AU Smith, Daniel J. [Reprint author]; King, William F.; Godiska, Ronald
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA,
02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 3135-3142. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB Active immunization with Streptococcus mutans **glucan binding protein B** (GBP-B) has been shown to induce protection against experimental dental caries. This protection presumably results from continuous secretion of salivary antibody to GBP-B, which inhibits accumulation of *S. mutans* within the oral biofilm. The purpose of this study was to explore the influence of short-term (9- or 24-day) passive oral administration of antibody to *S. mutans* GBP-B on the longer-term accumulation and cariogenicity of *S. mutans* in a rat model of dental caries. Preimmune chicken egg yolk immunoglobulin Y (IgY) or IgY antibody to *S. mutans* GBP-B was supplied in lower (experiment 1) and higher (experiment 2) concentrations in the diet and drinking water of rats for 9 (experiment 1) or 24 (experiment 2) days. During the first 3 days of IgY feeding, all animals were challenged with 5X10⁶ streptomycin-resistant *S. mutans* strain SJ-r organisms. Rats remained infected with *S. mutans* for 78 days, during which rat molars were sampled for the accumulation of *S. mutans* SJ-r bacteria and total streptococci. Geometric mean levels of *S. mutans* SJ-r accumulation on molar surfaces were significantly lower in antibody-treated rats on days 16 and 78 of experiment 2 and were lower on all but the initial (day 5) swabbing occasions in both experiments. Relative to controls, the extent of molar dental caries measured on day 78 was also significantly decreased. The decrease in molar caries correlated with the amount and duration of antibody administration. This is the first demonstration that passive antibody to *S. mutans* GBP-B can have a protective effect against cariogenic *S. mutans* infection and disease. Furthermore, this decrease in infection and disease did not require continuous antibody administration for the duration of the infection period. This study also indicates that antibody to components putatively involved only in cellular aggregation can have a significant effect on the incorporation of mutans streptococci in dental biofilm.